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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
PORTNER, V	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/252,691	Applicant(s) Weinstock
	Examiner Portner	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 22, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above, claim(s) *14-28* is/are withdrawn from consideration.

5) ☒ Claim(s) *42 and 46* is/are allowed.

6) ☒ Claim(s) *1-13, 29-41, 43-45, and 47-50* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-50* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Claims 1-50 are pending.

Claims 14-28 stand withdrawn from consideration.

Claims 1-13 and new claims 29-50 are under consideration.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Allowable Subject Matter

2. Claims 42 and 46 define over the prior art of record and are allowed.

Rejections Withdrawn

3. Claims 1,5,9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in light of the amendment of the claims to recite consistent open language.

4. Claims 1,5,10 are rejected under 35 U.S.C. 102(b) as being anticipated by Haertl, R et al (1993), in light of the amendment of the claims to define the isolated nucleic acid as a molecule other than chromosomal DNA.

5. Claims 1,5,10 are rejected under 35 U.S.C. 102(b) as being anticipated by Matsutani, S et al (1991), in light of the amendment of the claims to define the isolated nucleic acid as a molecule other than chromosomal DNA.

6. Claims 1,5,10 rejected under 35 U.S.C. 102(b) as being anticipated by Lambert-Zechovsky, N et al (1992), in light of the amendment of the claims to define the isolated nucleic acid as a molecule other than chromosomal DNA.

Rejections Maintained/Reinstated/Applied to New Claims

7. Claims 1-13 and new claims 29-41, 43-45, 47-50 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific, credible and substantial asserted utility or a well established utility for the elected invention of SEQ ID NO 7056 or SEQ ID No 1394 that encodes a polypeptide for reasons of record in paper number 14, paragraph 10.

8. Claims 1-13 and new claims 29-41, 43-45, 47-50 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, credible and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention for reasons of record in paper number 14, paragraphs 10 and 11.

9. Claims 11-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for probes and primers, the instant specification , does not reasonably provide enablement for gene therapy using the elected SEQ ID NO 7056. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims, in light of the fact that claim 12 recites an adjuvant and claim 13 contains a pharmaceutically active ingredients, thus defining claim 11 from which claims 12 and 13 as a pharmaceutical composition, a composition analogous to that of a vaccine.

10. Claims 5, 9, 29 (no specified size for the polypeptide) and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Blattner et al (January 29, 1997 (EMBL record, see sequence alignments **AE000213 and AAC74219**) or Oshima et al (1996,EMBL sequence alignments D90748 and BAA35957), in light of the disclosed sequence of Blattner sharing 100% sequence identity over at least 30 nucleic acids (encodes for 10 amino acids) and the claimed product is not so limited as being a E.cloace specific nucleic acid sequence.

Response to Arguments

11. Applicant's arguments filed June 22, 2001 have been fully considered but they are not persuasive.

12. The rejections of claims 2-4,6-8,11-13 under 35 U.S.C. 101 and 35 U.S.C. 112, first are argued by asserting that utility of the polypeptide has been established in the instant specification, in the annotation in Table 2, and the disclosed sequence.

13. It is the position of the examiner that at page 53, line 7, the sequences are asserted to have putative identification and function, Table 2 defines SEQ ID No 7056 as a hypothetical protein through reference to the "ymfc (b1135) gene" and not other specific descriptions could be found in the specification. The hypothetical protein of another bacteria by reference would define the instant sequence as a hypothetical protein in the absence of clarifying narrative.

The specific accession numbers P75966 were created November 1, 1997, but comment section appears to be dated November 23, 1998 and defines the hypothetical protein to be a member of the pseudouridine synthase family. The description was provided to the public about *ymfc* after the filing date of the instant specification. The EMBL database print out defines the accession number of Blattner to be a hypothetical protein, and the instant sequence is identified with reference to *ymfc*, and by correspondence to a hypothetical protein can be considered to be a hypothetical protein as well. At the time of filing, applicants hypothetical protein had not been identified with any specific biological activity.

14. Applicant provides a list of 6 different components that are asserted to define utility for the claimed products of the Amendment dated June 22, 2001, at section II, pages 7-8.

15. It is the position of the examiner that the:

primary structure of a putative polypeptide does not define the nucleic acid that encodes the polypeptide as a specific diagnostic agent and the polypeptide is not defined to have any specific function, just a putative structure.

Homology with other known polypeptides or nucleic acids does not define a nucleic acid as a specific diagnostic reagent, nor does it establish the polypeptides specific function. Applicant has provided evidence to this effect by submission of Exhibit B and the Koonin reference which shows conserved sequences for the encoded polypeptides. A nucleic acid molecule that would hybridize to a pseudouridine synthase open reading frame need not be specific to E. Cloacae, but would hybridize to any one of the other bacteria shown in Exhibit B or Koonin due the highly conserved sequences that encode the identical amino acid sequences.

While established data bases are invaluable in assisting molecular biologist in furthering research, the instant specification does not define the claimed nucleic acid as encoding a polypeptide of any known function based upon structural homology with other known sequences.

16. Applicant asserts that the claimed polypeptide is a pseudouridine synthase.

17. The examiner requests Applicant to point to the section of the instant specification that defines the claimed nucleic acid to encode a polypeptide with pseudouridine synthase biological activity. The examiner was unable to locate that portion of the instant specification that teaches SEQ ID No 1394 to encode a polypeptide or protein of SEQ ID No 7056 which has

pseudouridine synthase biological activity. Filing of an Application that teaches the polypeptide with this function could obviate the rejection made of record under 35 U.S.C. 101.

With respect to the Koonin et al reference submitted to define the biological significance of pseudouridine synthase biological activity, the examiner requests Applicant to point to that section of the instant specification that incorporates specific guidance and teaching that SEQ ID NO 1394 encodes a homolog of the protein disclosed by Koonin et al (1996). Koonin et al does not mention anything about E.cloacae what so ever in the reference. One of skill in the art would not have ascertained that the E.cloacae nucleic acid that encodes pseudouridine synthase biological activity was known in light of the disclosure provided by Koonin et al.

Exhibit A was noted by the examiner that Blattner et al provide information under the Comment section, [similarity] subsection, that the E.coli nucleic acid encodes a member of the pseudouridine synthase family. This annotation was not created until November 23, 1998, a date after the effective filing date of the instant specification which is February 1998. Therefore, Blattner did not describe the nucleic acid disclosed in 1997 as encoding a polypeptide having pseudouridine synthase biological activity until after Applicant's effective filing date of the instant specification.

Exhibit B was noted by the examiner to show conserved regions of known pseudouridine synthases, but E.cloace is not mentioned, the molecules are taught to vary in relative molecular

weight from 25 to 40 Kda and the consensus pattern shown is not discussed in the instant specification.

The PROSITE document amino acid sequence GRLD is taught to be conserved among pseudouridine synthases. Upon reconsideration of the oligomer search done by the examiner, it was found that a molecule that has ferritin binding activity contains this consensus sequence and is not a pseudouridine synthase (see WO96/41172 sequence alignment provided).

New Grounds of Rejection

Please Note: Upon reconsideration of the guidance and teaching of the instant specification with respect to SEQ ID No 7056 and 1394 and the disclosed nucleic acid sequences of the prior art, the following rejections are being made of record.

Claim Rejections - 35 U.S.C. § 112

18. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claims 10, 37-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is directed to an isolated nucleic acid that hybridizes to SEQ ID NO 1394 and encodes a biologically active polypeptide. What type of biological activity does not polypeptide have? The instant specification does not assign any specific biological activity to the polypeptide encoded by SEQ ID No 1394, so what is the biological activity claimed? The claimed nucleic acid molecule hybridizes to an open reading frame and therefore is the complement of the coding nucleic acid sequence. How can an anti-sense nucleic acid sequence encode a polypeptide and be contained on the same strand of DNA as SEQ ID No 1394? The claimed invention does not distinctly claim Applicant's invention.

Claim 37 is directed to a nucleic acid of any size that encodes a polypeptide of any size and has at least 90% sequence identity with SEQ ID No 7056. What is the size of the nucleic acid? What function does the polypeptide have? The invention is not distinctly claimed.

Claim 38 is directed to a nucleic acid of any size that encodes a polypeptide of any size and has at least 95% sequence identity with SEQ ID No 7056. What is the size of the nucleic acid? What function does the polypeptide have? The invention is not distinctly claimed

21. Claims 29, 33, 37-38 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid sequence SEQ ID No 1394 for the detection

of E.cloacae in a sample, does not reasonably provide enablement for the use of any nucleic acid that only shares 70% sequence identity with SEQ ID No 1394, based upon nucleic acid changes encompassed by claiming the isolated nucleic acid sequence by SEQ ID No 7056. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use a nucleic acid sequence that only shares 70% sequence identity with SEQ ID 1394, the invention commensurate in scope with these claims.

The specification discloses an isolated nucleic acid sequence of SEQ ID No 1394 that was obtained from a pathogenic bacteria and is useful for the detection of the presence or absence of the pathogen in a sample.

A nucleic acid sequence claimed based upon an amino acid sequence permits up to 30% sequence differences over the entire length of the nucleic acid sequence, in light of degenerate codons. As the specification does not teach what function the polypeptide has, or regions of the nucleic acid can be changed, or are conserved and specific to E.cloacae differences in nucleic acid sequence of 30% would not predictably detect E.cloace under low stringency conditions because no specific guidance has been provided as to where changes in the nucleic acid sequence can be made to permit the nucleic acid sequence specifically detect E.cloace in a sample. No specific utility has been disclosed for the claimed polypeptide, and nucleic acid sequences claimed based upon a polypeptide amino acids sequence that has not been described in such a way as to define the polypeptide as being E.cloace specific would not predictably detect E.cloace in a sample, when the nucleic acid sequence evidences changes of up to 30%.

In support for the position, Blattner et al (reference of record) discloses a nucleic acid sequence that shares 100% sequence identity with SEQ ID No 7056 over 185 nucleic acids, wherein the nucleic acid sequence was obtained from E.coli and encodes over 50 amino acids that share 100% identify with SEQ Id No 7056. Thus a nucleic acid claimed based upon the recited amino acid sequence would not be predictably detect E.cloace specific and would therefore not permit the person of skill in the art to use the claimed nucleic acid to detect E.cloace in a sample with any certainty in light of the nucleic acid sequence taught in the prior art that shares such a high degree of homology with the claimed sequence.

Absent specific guidance in the instant specification, the person of skill in the art would not be able to make and use a nucleic acid to predictably detect E.cloace which shares about 67 % sequence identity with SEQ ID 1394, or a sequence of any size that shares 90% or 95% with SEQ ID No 7056 because where and how the nucleic acid sequence could be changed and still predictably detect E.cloace has not been described, and the claimed nucleic acid can be any size and is a sequence that shares the recited percentage identity of that portion of SEQ ID No 7056 to which it corresponds because the size of the nucleic acid molecule is not specified. No nucleic acid sequences that are specific to only E.cloace are specifically claimed.

Conclusion

22. This is a non-final action.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.
Vgp
September 20, 2001

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